Summary of the Invention

The subject matter of this invention is directed to that field which has become known as "laser capture microdissection." In its original format, laser capture microdissection is described in Liotta et al. United States Patent 5,843,657 , et al. issued December 1, 1998. In that disclosure, a process of microdissection is disclosed. A sample having a portion for microdissection is contacted with a selectively activatable transfer surface. In its original state, the transfer surface is not adhesive to the sample. The sample is visualized for the portion of the sample it is desired to microdissect, this visualization typically being through the transfer surface (which preferably is transparent). Thereafter, the transfer surface is activated only at the portion of the transfer surface overlying the portion of the sample for microdissection. The activated portion of the transfer surface adheres to the sample portion. The non activated portion of the transfer surface does not adhered to the sample. When the transfer surface is removed, the sample portion adheres to the transfer surface portion and is removed. The microdissection occurs.

Understanding that this is the field in which this disclosure resides, the claimed elements of claim 35 can be summarized.

First, and as set forth in the preamble to claim 35, the disclosed apparatus is limited to laser capture microdissection.

Second, what we deal with here is a convex surface for placement to a sample. (Please note that the surface is not concave.)

Third, the convex surface is mounted to an extremity of the rod.

Forth, a selectively activated coating is placed over the convex surface. Like the transfer surface of Liotta et al.' 657, the selectively activated coating has non adhesive properties. When activated this coating provides selected regions thereof with adhesive properties when placed to a sample. Non activated regions thereof remain with

their non adhesive properties. Using such a coating on a convex surface, laser capture microdissection can occur.

References Distinguished

First, the rejection has cited Liotta et al. United States Patent 5,843,644. This patent is the disclosure from which laser capture microdissection evolved. Specifically, Liotta et al.' 657 was a Continuation-in-Part of the Liotta et al.' 644. It was in that disclosure that laser capture microdissection was first set forth.

Attention is respectfully directed to an important limitation appearing in the Liotta et al.' 657 Patent appearing at column 4, lines 35 through 41 as follows:

> ... As can be readily understood from Fig. 2a, the surface area of the contact probe tip (and the adhesive/extraction reagent) needs to be about equal to, and no greater than and, the surface area of the zone to be extracted. Otherwise, excessive removal of adjacent tissue zones will occur.

This limitation takes the reference outside of the claimed invention of claim 35. Specifically, the selectively activated coating has non adhesive properties when originally placed over the convex surface. It is then "activated." The activation quality requires that the activated portion become the adhesive while the rest of the surface which is non activated remains non adhesive. This is not the case illustrated in Fig. 2c of Liotta et al.' 644. The reason for this is clear. Laser capture microdissection had not been disclosed to the world by the inventive team in Leota et al.' 657 (it being noted in Dr. Robert Bonner was named as an additional inventor in this latter disclosure).

Second, the rejection has cited Adams et al. (U.S. Patent 6,060,288). The rejection calls to applicant's attention cols. 16 lines 1 to 40 of Adams et al.' 288, portions of which are quoted here for convenience:

> ... Thus, the use of an optical fiber performs a three-fold function as the support for the amplification reaction, as a transmission means for the resultant signal and as a component of the detection system by transmitting this signal to the detector. [16: 7 to 12]

It can be seen from the above that dissection, let alone microdissection, is not a purpose of this disclosure. No mention of dissection is made.

But the disclosure continues further:

> One end of the optical fiber (referred to hereinafter as the distal end) is cleaved, polished, and then chemically modified to provide a surface having attachments sites for nucleic acid primers. A number of surface modification methods suitable for this purpose are known to those of skill in the art. For example, organosilane coating of glass and silica surfaces, ground polymerization on polymer surfaces, and/or high-voltage gas-plasmid discharges may be used to affect modification of glass, silica or polymer surfaces. The surface of the fiber may also be modified to have a convex or concave curvature to facilitate optical focusing. Following modification, oligonucleotides are then attached to the surface of the distal end of the fiber.

This process usually involves several steps, which may include one are more of the following:

a) Chemical treatment of the fiber surface to activated attachments sites for primer binding;

b) Chemical treatment of the oligonucleotides to activate the groups which will interact with the fiber surface sites;

c) Placing the modified fibers in contact with the oligonucleotides to allow immobilization reactions to occur; and,

d) Treatment hand washing of the fiber surfaces to remove non-immobilized oligonucleotides, as well as any activation reagents or blocking groups that may interfere with the amplification reaction. (Emphasis added)

Reviewing the above quotation, the first thing to note is that the fiber and its distal end is "cleaved." "Cleave" is defined as:

cleave 1 [kleev] (past cleaved, cleft [kleft], clove [kl v], past participle cleaved, cleft, clo•ven, present participle cleav•ing, 3rd person present singular cleaves) transitive and intransitive verb

1. split: to split, or make something split, especially along a plane of natural weakness

2. cut a path through: to make a way through something (literary) " We watched the bows of the tall ships cleave through the waves."

3. penetrate: to penetrate or pierce something deep or dense such as water or heavy undergrowth

[Old English cl ofan . Ultimately from an Indo-European word that is also the ancestor of Greek gluphein· "to carve" (source of English hieroglyphics).] (Microsoft Encarta Dictionary; Copyright 2002)

Applying this definition, the (distal) end of the optical fiber would look much like a cleaved branch having discrete separated "cleaved" portions splayed upwardly from the end of the optical fiber.

Second, chemical modification is undertaken. There is no indication that one portion of the distal fiber end is chemically treated while other portions of the distal fiber end are not chemically treated.

Then a statement is made about "the surface" of the fiber being given either concave or convex "to facilitate optical focusing." Insofar as this relates to the "cleaved distal end," it is not understood. How a cleaved end of the fiber can at the same time be provided with either a concave or a convex surface is not known. The only intelligible interpretation of the surface is that it is somewhere on the fiber where light enters or exits the fiber.

Further, the reference - concerned with optics - suggests either concave or convex - interchangeably. In this disclosure, concave will not work; only convex is operative. Optics is obviously the only consideration; dissection is not considered.

One thing is clear. The reference teaches that oligonucleotides are attached at the cleaved distal end of the reference *en mass*. It would seem that the

attachment of oligonucleotides to one portion of the distal end without attachment to other portions of the distal end is not at all contemplated. Further, dissection (especially microdissection) is never referred to anywhere in the reference.

These statements are not directed at the "intended use" of the product. Instead, they point out that the claim limitations are not met by the reference insofar is it refers to "convex surface for placement to a sample" and "a selectively activated coating placed over the convex surface having non adhesive properties which can be activated to provide selected regions thereof with adhesive properties when placed to a sample while non activated regions thereof remain with the non adhesive properties."

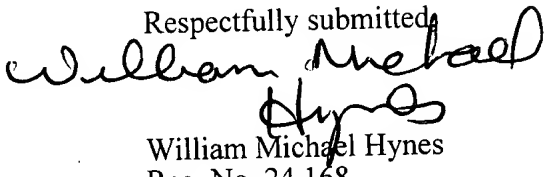
Finally, and principally because of the "cleaved" description of the distal end, it is not seen how over Adams et al. the claimed invention of claims 35 and 41 would be "obvious" within the meaning of 35 USC 103, especially where these surfaces are mentioned with respect to optics and the optically reversible concepts of "concave or convex" are used.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at .

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

35. (Once Amended) In an apparatus for laser laser capture microdissection, a contact surface comprising:

a convex surface for placement to a sample;

a rod with the convex surface mounted to an extremity of the rod; and,

a selectively activated coating placed over the convex surface having non adhesive properties which can be activated to provide selected regions thereof with adhesive properties when placed to a sample while non activated regions thereof remain with the non adhesive properties.

41. (Once Amended) In an apparatus for laser capture microdissection, a contact surface and vial comprising:

a convex surface;

a selectively activated coating placed over the convex surface having non adhesive properties which can be activated to provide selected regions thereof with adhesive properties when placed to a sample while non activated regions thereof remain with the non adhesive properties;

a vial having a dimension for permitting the convex surface to be placed into vial; and,

a fluid in the vial for liberating at least part of the tissue sample adhered to the selectively activated convex surface.